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				Application Number	10/567,630-Conf. #2853		
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S	TATEMENT I	3Y /	APPLICANT	First Named Inventor	Kari Alitalo		
				Art Unit	<b>ңқққ 1634</b>		
	(Use as many sh	eets a	s necessary)	Examiner Name	******* Kapushoc		
Sheet	1	of	4	Attorney Docket Number	28113/39467A		

	U.S. PATENT DOCUMENTS								
Examiner	Cite	Document Number	Publication Date	Name of Patentee or	Pages, Columns, Lines, Where				
Initials*	No 1	Number-Kind Code <sup>2</sup> ( # known)	MM-DD-YYYY	Applicant of Cited Document	Relevant Passages or Relevant Figures Appear				
	A1*	US-4,946,778	08-07-1990	Ladner et al.					
	A2*	US-5,093,246	03-03-1992	Cech et al.					
	A3*	US-5,116,742	05-26-1992	Cech et al.					
	A4*	US-5,225,337	07-06-1993	Robertson et al.					
	A5*	US-5,254,678	10-19-1993	Haseloff et al.					
	A6*	US-5,939,598	08-17-1999	Kucherlapati et al.					
	A7*	US-2003/087807	05-08-2003	Greenspan R. J.					

FOREIGN PATENT DOCUMENTS										
Examiner Initals*	Cite No	Foreign Patent Document  Country Code <sup>5</sup> -Number <sup>4</sup> -Kind Code <sup>6</sup> (#known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T^				
	B1	WO 90/07641	07-12-1990	Sundstrand Corporation		$\vdash$				
	B2	WO 93/23569	11-25-1993	Ribozyme Pharmaceuticals, Inc.		Г				
	B3	WO 94/02602	02-03-1994	Cell Genesys, Inc.		$\vdash$				
	B4	WO 96/33735	10-31-1996	Cell Genesys, Inc.						
	B5	WO 96/34096	10-31-1996	Cell Genesys, Inc.		T				
	B6	WO 00/32765	06-08-2000	Immusol, Inc.		-				
	B7	WO 03/27285	04-03-2003	Bionomics Ltd.		-				

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		NON PATENT LITERATURE DOCUMENTS	
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	C1	Artavanis-Tsakonas, Notch Signaling: Cell fate control and signal integration in development. Science, Vol. 284, pp.770-776 (1999).	-
	C2	Bach et al., Stem cells: The intestinal stem cell as paradigm. Carcinogenesis, Vol. 21, pp.469-476 (2000).	
	C3	Bange et al., Cancer progression and tumor cell motility are associated with the FGFR4 Arg388 allele. Cancer Res., Vol. 62, pp.840-847 (2002).	-
	C4	Brummelkamp et al., A system for stable expression of short interfering RNAs in mammalian cells. Science, Vol. 296, pp.550-553 (2002).	
	C5	Cavallaro et al., N-CAM modulates tumour-cell adhesion to matrix by inducing FGF-receptor signaling. <i>Nat. Cell Biol.</i> , Vol. 3, pp.650-657 (2001).	
	C6	Chowrira et al., Extensive phosphorothioate substitution yields highly active and nuclease- resistant hairpin ribosymes. <i>Nucleic Acids Res.</i> , Vol. 20, pp.2835-2840 (1992).	-
	C7	Cote et al., Generation of human monoclonal antibodies reactive with cellular antigens. Proc.	2000333

Date

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Approved for use through 0331007 CMB good to 
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S	TATEMENT E	3Y /	APPLICANT	First Named Inventor	Kari Alitalo	
				Art Unit	1638 1634	
	(Use as many sheets as necessary)			Examiner Name	ANNEXWENCE Kapushoc	
Sheet	2	of	4	Attorney Docket Number	28113/39467A	

	Natl. Acad. Sci. (USA), Vol. 80, pp.2026-2030 (19				
C8	Daubendiek et al., Generation of catalytic RNAs nanocircles. Nat. Biotechnol., Vol. 15, No. 3, pp.2	273-277 (1997).			
C9	Elbashir et al., RNA interference is mediated by 2 Vol. 15, pp.188-200 (2001).				
C10 Elbashir et al., Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells. Nature, Vol. 411, pp.494-498 (2001).					
C11	(USA), Vol. 91, pp.664-668 (1994).				
C12					
C13	Fingl et al., Chapter 1: General Principles. "The F (1975).	Pharmacological Basis o	f Therapeutics," pp.1		
C14	Fire et al., Potent and specific genetic interference elegans. Nature, Vol. 391, pp.806-811 (1998).	e by double-stranded R	NA in Caenorhabditis		
C15	Fujimori et al., Regulation of lipocalin-type prosta 1 through E-box and interleukin-1β via two NF-κE Chem., Vol. 278, pp.6018-6026 (2003).	B elements in rat leptom	eningeal cells. J. Biol.		
C16	Giles et al., Caught up in a WNT storm: Wnt sign: 1653, pp.1-24 (2003).	-			
C17	Gupta et al., Colorectal cancer prevention and tre Nat. Rev. Cancer, Vol. 1, pp.11-21 (2001).				
C18					
C19	Hutvagner et al., A microRNA in a multiple-turnover RNAi enzyme complex. Science, Vol. 29 pp.2056-2060 (2002).				
C20	Jensen et al., Control of endodermal endocrine development by Hes-1. Nat. Genet., Vol. 24, pp.36-44 (2000).				
C21	Jordan et al., Expression of functional CXCR4 che epithelial cells. J. Clin. Invest., Vol. 104, pp.1061-	1069 (1999).			
C22	Joutel et al., Notch3 mutations in CADASIL, a her and dementia. Nature, Vol. 383, pp.707-710 (1990)	6).	-		
C23	Kaneda et al., Increased expression of DNA coint Science, Vol. 243, pp.375-378 (1989).				
C24	Kato et al., Expression of hepatitis B virus surface 266, pp.3361-3364 (1991).				
C25	Kawasaki et al., Hes1 is a target of microRNA-23 differentiation of NT2 cells. Nature, Vol. 423, pp.8	38-842 (2003).			
C26	Koizumi et al., Design of RNA enzyme distinguish Acid Res., Vol. 17, pp.7059-7071 (1989).	ing a single base mutat	ion in RNA. Nucleic		
C27	Kurreck et al., Design of antisense oligonucleotides stabilized by locked nucleic acids.  Nucleic Acids Res., Vol. 30, pp.1911-1918 (2002).				
C28	Ladner et al., dUTP nucleotidohydrolase isoform tissues: association with survival and response Cancer Research, Vol. 60, pp.3493-3503 (2000).	to 5-fluorouracil in cole	orectal cancer.		
C29	Lee et al., Expression of small interfering RNAs human cells. Nat. Biotechnol., Vol. 20, pp.500-50	targeted against HIV-1 5 (2002).	rev transcripts in		
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Sheet	3	of	4	Attorney Docket Number	28113/39467A	

C30	Li et al., Alagille syndrome is caused by mutations in human Jagged1, which encodes a ligand for Notch1. Nature Genet., Vol. 16, pp.243-251 (1997).	Г
C31	Lima et al., Combinatorial screening and rational optimization for hybridization to folded hepatitis C virus RNA of oligonucleotides with biological antisense activity. J. Biol. Chem., Vol. 272, pp.626-638 (1997).	
C32	Long et al., Self-cleaving catalytic RNA. FASEB J., Vol. 7, pp.25-30 (1993).	
C33	Martinez et al., Single-stranded antisense siRNAs guide target RNA cleavage in RNAi. Cell, Vol. 110, pp.563-574 (2002).	
C34	Morrison et al., Chimeric human antibody molecules: mouse antigen-binding domains with human constant region domains. <i>Proc. Natl. Acad. Sci. (USA)</i> , Vol. 81, pp.6851-6855 (1984).	
C35	Nagahara et al., Transduction of full-length TAT fusion proteins into mammalian cells: TAT-p27Kip1 induces cell migration. Nature Medicine, Vol. 4, pp.1449-1452 (1998).	
C36	Nicolau et al., Liposomes as carriers for in vivo gene transfer and expression. <i>Methods Enzymol.</i> , Vol. 149, pp.157-176 (1987).	
C37	Ojwang et al., Inhibition of human immunodeficiency virus type 1 expression by a hairpin ribozyme. <i>Proc. Natl. Acad. Sci. (USA)</i> , Vol. 89, pp.10802-10806 (1992).	
C38	Palmer et al., Vitamin D(3) promotes the differentiation of colon carcinoma cells by the induction of E-cadherin and the inhibition of beta-catenin signaling. J. Cell Biol., Vol. 154, pp.369-387 (2001).	
C39	Perales et al., Gene transfer in vivo: sustained expression and regulation of genes introduced into the liver by receptor-targeted uptake. <i>Proc. Natl. Acad. Sci. (USA)</i> , Vol. 91, pp.4086-4090 (1994).	
C40	Perrotta et al., Cleavage of oligoribonucleotides by a ribozyme derived from the hepatitis delta virus RNA sequence. <i>Biochem</i> , Vol. 31, pp.16-17 (1992).	
C41	Petrova et al., Lymphatic endothelial reprogramming of vascular endothelial cells by the Prox-1 homeobox transcription factor. <i>Embo J.</i> , Vol. 21, pp.4593-4599 (2002).	
C42	Quaroni et al., p27(Kip1) is an inducer of intestinal epithelial cell differentiation. Am. J. Physiol. Cell. Physiol., Vol. 279, pp.C1045-1057 (2000).	
C43	Schwarze et al., In vivo protein transduction: delivery of a biologically active protein into the mouse. <i>Science</i> , Vol. 285, pp.1569-1572 (1999).	
C44	Sosa-Pineda et al., Hepatocyte migration during liver development requires Prox1. Nat. Genet., Vol. 25, pp.254-255 (2000).	
C45	Symons, Small catalytic RNAs. Ann. Rev. Biochem., Vol. 61, pp.641 (1992).	
C46	Takeda et al., Construction of chimaeric processed immunoglobulin genes containing mouse variable and human constant region sequences. <i>Nature</i> , Vol. 314, pp.452-454 (1985).	
C47	Tomita et al., Isolation and characterization of a highly malignant variant of the SW480 human colon cancer cell line. Cancer Res., Vol. 52, pp.6840-6847 (1992).	
C48	Tuschl, Expanding small RNA interference. Nat. Biotechnol., Vol. 20, pp.446-448 (2002).	
C49	Usman et al., Hammerhead ribozyme engineering. Current Opin. Struct. Biol., Vol. 6, pp.527-533 (1996).	
C50	van de Wetering et al., The beta-catenin/TCF-4 complex imposes a crypt progenitor phenotype on colorectal cancer cells. <i>Cell</i> , Vol. 111, pp.241-250 (2002).	
C51	White et al., Vascular endothelial growth factor-D expression is an independent prognostic marker for survival in colorectal carcinoma. Cancer Res., Vol. 62, pp.1669-1675 (2002).	
C52	Wigle et al., Prox1 function is required for the development of the murine lymphatic	

Examiner Signature	/Stephen Kapushoc/	Date Considered	01/12/2010
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Substitute for form 1449/PTO Complete if Known Application Number 10/567.630-Conf. #2853 INFORMATION DISCLOSURE Filing Date February 8, 2006 STATEMENT BY APPLICANT First Named Inventor Kari Alitalo 1634 Art Unit (Use as many sheets as necessary) Kapushoc \*\*\*\*\*\*\*\* Examiner Name Sheet Attorney Docket Number 28113/39467A

	system. Cell, Vol. 98, pp.769-778 (1999).
C53	Wigle et al., Prox1 function is crucial for mouse lens-fibre elongation. Nat. Genet., Vol. 21 pp.318-33 (1999).
C54	Wigle et al. An essential role for Prox1 in the induction of the lymphatic endothelial cell phenotype. <i>EMBO J.</i> 21:1505-1513 (2002).
C55	Yamada et al., Fibroblast growth factor receptor (FGFR) 4 correlated with the malignancy of human astrocytomas. <i>Neurol Res.</i> , Vol. 24, pp.244-248 (2002).
C56	Yang et al., Targeted inactivation of the p21(WAF1/cip1) gene enhances Apc-initiated lumor formation and the tumor-promoting activity of a Western-style high-risk diet by altering cell maturation in the intestinal mucosal. Cancer Res., Vol. 61, pp.565-569 (2001).
C57	Yang et al., Requirement of Math1 for secretory cell lineage commitment in the mouse intestine. Science, Vol. 294, pp.2155-2158 (2001).
C58	Yu et al., RNA interference by expression of short-interfering RNAs and hairpin RNAs in mammalian cells. <i>Proc. Natl. Acad. Sci.</i> (USA), Vol. 99, pp.6047-6052 (2002).
C59	Zeng et al., Both natural and designed micro RNAs can inhibit the expression of cognate mRNAs when expressed in human cells. <i>Mol. Cell</i> , Vol. 9, pp.1327-1333 (2002).
C60	International Preliminary Report on Patentability, PCT/EP2004/008819, dated February 13, 2006.

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